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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/681,753	05/31/2001	James Norman Cawse	RD-28169	6423

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/681,753

Applicant(s)

CAWSE, JAMES NORMAN

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 13-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 13-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

ACTION DETAILED

Applicants' arguments, filed 23 July 2003, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-9 and 13-26 are currently pending in the application.

Declaration Under 37 CFR § 1.132

The declaration submitted 23 July 2003 is acknowledged.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Non-Statutory Subject Matter

Claims 1-9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to **non-statutory subject matter**. The method to conduct an experiment, which incorporates selecting, estimating, assigning, effecting, and adjusting data, is only mathematical manipulation of that data. A method which identifies drug candidates for further testing (e.g. from a combinatorial library) MAY be one which produces a concrete, tangible, and useful result. However, some knowledge is required with regard to a specific receptor and/or disorder or disease for which the candidate compounds are to be screened. In the instant claims, there is no

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specificity identified as to what is intended by the outcome of the method, Therefore, the invention does not meet the standard of being immediately useful. Furthermore, there is no particular data identified or specific factors recited in the specification such that a concrete, tangible, useful result is readily apparent. The specification is devoid of information on a possible correlation of this method to a particular disease or disorder, for example. There is no recitation of what to do with the probabilities generated or how that result of the method is concrete, tangible or useful.

As set forth in MPEP 2106: “For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See *Alappat*, 33 F.3d at 1543, 31 USPQ2d at 1556-57 (quoting *Diamond v. Diehr*, 450 U.S. at 192, 209 USPQ at 10). See also *Alappat* 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) (“unpatentability of the principle does not defeat patentability of its practical applications”) (citing *O’Reilly v. Morse*, 56 U.S. (15 How.) at 114-19). A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible, and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible, and useful. See *AT&T*, 172 F.3d at 1358, 50 USPQ2d at 1452. Likewise, a machine claim is statutory when the machine, as claimed, produces a concrete, tangible, and useful result (as in *State Street*, 149 F.3d at 1373, 47 USPQ2d at 1601) and /or when a specific machine is being claimed (as in *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557 (in banc).”

Furthermore, not all processes are statutory under 35 USC 101, as put forth in *Schrader*, 22 F.3d at 296, 30 USPQ2d at 1460. To be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical

application in the technical arts is either disclosed in the specification or would have been known to the skilled artisan or (B) be limited to a practical application within the technological arts.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 13-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and all claims dependent there from recite a method to conduct an experiment comprising selecting factors, estimating interaction, assigning probabilities, effecting an experiment, and adjusting probabilities. The step of effecting a CHTS method on an experimental space representing the levels, wherein the CHTS method comprises defining a first experimental space by structuring the levels according to Latin Square strategy is unclear. It appears that factors are selected and interactions estimated so that an experimental space may be designed. A Latin Square model structures the experimental space and **then** a CHTS experiment is conducted (see summary of invention, page 3 of specification). However, the confusion lies in the claims language because the claim implies that the physical steps of CHTS are somehow tied to a Latin Square model, rather than the space being designed by the model and then an experiment conducted. Claim 13 leads to further confusion in this matter because there are different steps for the CHTS method. Does the experiment comprise Latin Square models or does it comprise formulating a combinatorial library? The question is which method does applicant intend? Clarification of the virtual versus the physical steps is requested.

Claims 2 and 4 recite limitations of the probability values, such as high, medium, and low, and limitations on the method of claim 1. Does applicant intend the claim to limit the probability values or does applicant intend to limit the method to assignment by a client or investigator? Clarification is requested.

Claim 3 is grammatically incorrect, as it does not contain a verb. It is unclear what is intended by this claim.

Claim 9 recites the phrase "an adjustable definition model". It is not clear from the claim or the specification what this means. Does the model somehow relate to the experimental space? Is the model the actual experimental space? What is the model defining?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 13-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,901,069 (Agrafiotis et al.), in view of Reddington et al (Science (1998) Vol. 280, pages 1735-1737), in further view of Milliken et al. (Analysis of Messy Data Volume I: Designed Experiments (1992) Chapman and Hall Publishing, page 47 and 61).

Agrafiotis et al. describes a computer-based, iterative process for generating chemical entities with defined physical chemical and/or bioactive properties (see abstract). Specifically, a synthesis protocol generator is used to identify, under computer control, reagents which when combined with one another will produce compounds which are predicted (by structure-activity models) to exhibit improved activity properties, test the validity of the current structure-activity models, and discriminate between various structure-activity models (column 6, lines 36-44). The synthesis protocol generator classifies compounds which possess the desired activity/properties as new leads. After selection of factors, the experiment is run such that it may be adjusted based upon parameters that include assigning values to properties attained and adjusting the experiment for further iterations based upon adjustments (see column 6, lines 46-67; see also, column 13, lines 31-59 pertaining to predictions). (Claim 1)

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A preferable embodiment of Agrafiotis is one in which the protocol generator assigns a rating factor to each compound based upon how closely the compound's activity/properties match a desired profile. The rating factors may be numerical (as is true in the instant application) or linguistic values. Furthermore, these values are represented on a sliding scale from high to low values which correspond to the activity/property profile (column 16, lines 39-54). (Claims 1-3, 5-9) In addition to the above embodiments meeting the limitations of said claims, the inputs of the disclosed invention are user determined (column 7, line 25-27). (Claims 2, 4). The invention is performed by a chemical synthesis robot which gains its instructions from the synthesis protocol generator. The robot is capable of mix-and-split solid phase chemistry and performs selective microscale synthesis of the specific combinatorial library on a reaction plate (column 8, lines 31-56).

Agrafiotis et al. do not teach a combinatorial screening method in parallel, as in claim 13, nor do they teach specific use of inorganic catalysts (although the invention is useful for a myriad of applications as acknowledged at column 5, lines 51-61). However, Reddington et al. do disclose a combinatorial screening method to select the best catalysts (page 1735, column 2, lines 4-14 and page 1736, column 1, lines 17-21), including ternary array combinations and parallel screening (page 1735, column 3, lines 27-29). Reddington et al. describe the need for well designed arrays, some of which contain complexes such as ruthenium and platinum, meeting the limitation of claim 21, 24, and 25 (page 1736, column 3, lines 8-10). They also mention a halide composition at page 1736, column 3, line 9, as in claim 23. While not mentioning palladium (claim 22), it would be obvious to substitute any of the Group VIII B

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metals in this method. Furthermore, the method includes the use of fluorescent indicators, as in claim 17 (tags).

Agrafiotis et al. do not teach the specific experimental design using the Latin Square modeling technique, however, Milliken et al. do teach this method for experimental design (page 47).

“Properly designed and analyzed experiments provide the maximum amount of information about the conditions investigated for the resources used. The design structures presented include the completely randomized, randomized complete block, Latin Square, and incomplete block design....Experimental design is concerned with the planning experiments in order to obtain maximum amount of information from the available resources. Often when designing an experiment, the experimenter has control over certain effects called treatments, populations, or treatment combinations. The experimenter generally controls the choice of the experimental units and whether or not those experimental units need to be put into groups, called blocks”.

At page 61 he states that the Latin Square model is very useful for implementing an experiment when there is a need for a block design in two directions.

One of ordinary skill in the art at the time of the invention would have been motivated to combine the teachings of Agrafiotis et al., who suggest that this method is applicable to many applications such as, generating chemical compounds having desired properties that may include paints, finishes, plastics, scents, flavorings, drugs, surfactants, etc. (column 5, lines 51-61), with the methods of Reddington et al., who teach inorganic catalysis and parallel processing. The motivation is provided by Agrafiotis at column 21, where he states that in an alternative embodiment of the invention a plurality of systems operate in parallel to generate and analyze lead compounds (lines 35-37).

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It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention would to combine the teachings of Agrafiotis et al. and Reddington et al. and the Latin Square model of Milliken. Agrafiotis provides the motivation to do so at column 17, where he states that other suitable metrics (besides those in the invention) may be used for the statistical analysis (lines 65-67).

No claims are allowed.

Inquiries

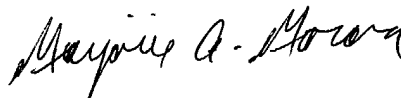
Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

MARJORIE MORAN
PATENT EXAMINER



December 13, 2003

Lori A. Clow, Ph.D.

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